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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/235,986	01/22/99	HENDRICKSON W	58323/JPW/PT

NM12/1023

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EXAMINER	
ALLEN, M	
ART UNIT	**PAPER NUMBER**
1631	22

DATE MAILED: 10/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/235,986	HENDRICKSON ET AL.	
	Examiner	Art Unit	
	Marianne Allen	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed 8/17/01 is noted and has been entered.

Upon further consideration of the specification, the claims, and applicant's response, finality of the previous Office action (Paper No. 15, mailed 6/18/01) is hereby withdrawn in favor of the non-final Office action set forth below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-12 are under consideration by the examiner.

Request for Information under 37 CFR 1.105

Applicant is requested to provide any material (printed, electronic, etc.) of which they are aware concerning the Argonne National Laboratory (ANL) meeting held in January 1998 to discuss issues related to a genome-directed Protein Structure Initiative (PSI).

Applicant is requested to provide any material (printed, electronic, etc.) of which they are aware concerning the National Institute of General Medical Sciences (NIGMS) meeting held on April 24, 1998, to discuss issues related to a genome-directed Protein Structure Initiative (PSI).

Applicant is requested to provide any material (printed, electronic, etc.) of which they are aware concerning the National Institute of General Medical Sciences (NIGMS) meeting held on November 24, 1998, to discuss issues related to a genome-directed Protein Structure Initiative (PSI).

Applicant was present at the meetings on 4/24/98 and 11/24/98 and it is likely that applicant was present at the meeting in January 1998. Material concerning the genome-directed

Protein Structure Initiative might function as 102(a) or (b) art against the instant application in view of applicant's filing date of 22 January 1999 and is germane to the instant claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-12 are rejected under 35 U.S.C. 102(a) as being anticipated by the National Institute of General Medical Sciences (NIGMS) Protein Structure Initiative (PSI) Meeting Summary dated 4/24/98.

This document summarizes the discussion of a one-day meeting held on 24 April 1998 to experimentally determine 3D structures of protein families via a representative protein molecule (target) from each family. The text of the document was last updated 2 June 1998. (See page 20 of document, last line.) Protein sequences were compared using sequence homology to define families and targets selected. The targets are then cloned into plasmids for overexpression, and purified for use in crystallization trials. Those targets successfully crystallized have X-ray crystallography and protein structure determination performed. Synchrotrons, multiwavelenth anomalous diffraction (MAD), and selenomethionyl enrichment are specifically disclosed. Structural and functional properties would be predicted. In particular, identification of protein fold motifs is disclosed. The results of the analysis is put in a database with any additional information that may be helpful for further experiments. The database is updated and annotated

as research progresses. The database is intended to be accessible to all researchers. (See in particular pages 4-15 of document.) Implicit in this document is a system containing the component parts (database and means) for executing each of the steps of the method. It is noted that while at least inventor Hendrickson is indicated to have been present at the meeting (see page 18), the document cannot be considered his own work as it represents the recommendations and conclusions of all participants.

Claims 1-12 are rejected under 35 U.S.C. 102(a) as being anticipated by Gaasterland (Nature Biotechnology, July 1998).

Gaasterland reviews the goals and initial results of the structural genomics initiative. Results from the pilot project presented in January 1998 at the Argonne National Laboratory are discussed. Flow diagrams (Figures 1 and 2) and particular bioinformatics tools (Table 1) with the accompanying discussion are considered to disclose the claimed methods and system.

Claim Rejections - 35 USC § 112

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some aspects of the claimed method and system, does not reasonably provide enablement for the breadth of what is encompassed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims encompass use of a synchrotron. Such a piece of equipment is not readily available for use or purchase. Note that beamline time must be applied for at existing

synchrotron facilities such as Argonne National Laboratory and that a synchrotron is not readily available for purchase. See Holmes (Philosophical Transactions of the Royal Society of London Biological Sciences, December 1999) which establishes that synchrotrons cost approximately $100,000,000.00, take approximately 10 years to build, and can't be purchased from a catalog. Holmes also documents that there are only a limited number of synchrotron facilities in the world.

With respect to clustering sequences into families, Heger et al. (Progress in Biophysics & Molecular Biology, 2000) establishes that even well after the filing date, this was a non-trivial computational problem. Note family assignment in structural genomics is specifically discussed at pages 334-335 and that in February 1999 (after the instant filing date) target lists of unknown protein families were still being developed.

The claims encompass any and all proteins and families, yet it would have been well known in the art at the time of the invention that membrane bound, proteins found in complexes, and insoluble proteins were problematic for crystallization and X-ray crystallographic structure determination. Note that the pilot projects for structural genomics as discussed by Gaasterland were selected in part to determine what classes of proteins were feasible to attempt structure determinations upon and were selected because they were thought to be easier.

To the degree that the system of claims 1-6 is directed to an integrated, turn-key system or fully automated system with the recited database and various recited means, such systems are not enabled. The examiner is not aware of any integrated system or fully automated system possessing all (or even most) of the recited components at the time of the invention. Even particular aspects of the system were not fully automated. For example, it does not appear that

crystallization apparatus (to produce suitable crystals from proteins) was integrated to or automated in association with a synchrotron at the time of the invention nor would it have been feasible to do so. The crystals would have been grown and stored until such time as the synchrotron was available for diffraction analysis. It is deemed undue experimentation to practice this embodiment of the invention.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite "information for selected proteins." However, it is unclear how a protein is selected (what parameters or criteria are used) and how many proteins are selected. That is, the metes and bounds of this selection cannot be determined.

The claims recite "homologous sequences." However, it is unclear what level of homology is required to meet the limitation of the claim.

The claims recite "a plurality of target proteins which are members of the family." However, the criteria that define a family are not provided. It is unclear how a target is selected (what parameters or criteria are used) and how many targets are selected.

The claims recite "screening products of the synthesis to choose selected synthesized products for processing." However, the criteria or parameters for the selection are not provided.

The claims recite "crystallization screens." However, the meets and bounds of what is screened and what information is used or produced is not set forth or defined.

The claims recite "suitable specimen crystals." However, it is unclear what is required to meet the limitation of "suitable." That is, the metes and bounds of this term are not provided.

The claims recite updating the database without providing a clear direction as to what is updated. That is, are new entries created and added to the database, fields added, fields edited or annotated, or is something else intended? Is the updating with respect to each and every target or with respect to the predicted class of compounds (each and every predicted compound?) and/or homology model of predicted protein structures and/or something else?

Claims 1 and 7 recite "binding potency using the active sites information corresponding to the target protein." This is confusing as the target may or may not have binding potency (whatever the metes and bounds of this phrase may be which are not defined) nor any active sites (again the metes and bounds of what would meet this limitation is not provided). It is unclear exactly what is being modeled in the portions following this phrase. It appears it could be either proteins similar to the target (in the same family) or proteins that bind to or interact with the target.

With respect to claims 1-6, the claimed system does not set forth the relationship of the database, bioinformatics tool, protein synthesis means, protein processing means, crystallization means, X-ray crystallography means, and so forth. That is, the claim language does not reflect an integrated or turn-key system where the components are related or linked to each other in some fashion. As written, the claim appears to be directed to a collection of laboratory equipment or machines. This does not appear to define a system.

With respect to claims 7-12, the claimed method fails to particularly point out what steps are to be performed and how they are to be performed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 703-308-0666. The examiner can normally be reached on Monday-Friday, 9:00 am - 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703-308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Marianne P. Allen
Primary Examiner
Art Unit 1631

mpa
October 12, 2001